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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/539,178	01/23/2006	Kevin M. Flanigan	21101.0047U2	2241
23859 7590 01/24/2008 NEEDLE & ROSENBERG, P.C. SUITE 1000 999 PEACHTREE STREET ATLANTA, GA 30309-3915			EXAMINER STRZELECKA, TERESA E	
			ART UNIT 1637	PAPER NUMBER
			MAIL DATE 01/24/2008	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/539,178	FLANIGAN ET AL.	
	Examiner	Art Unit	
	Teresa E. Strzelecka	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 June 2008 and 05 November 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|----------------------------------------------------------------------------------------|-------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>12/19/05; 1/22/07; 5/7/07</u> . | 6) <input checked="" type="checkbox"/> Other: <u>Notice to Comply</u> . |

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I (claims 1-18, species of the dystrophin gene) in the reply filed on June 29, 2007 is acknowledged. The traversal is on the ground(s) that there would be no serious search and burden to examine the two groups together. This is found persuasive, therefore Groups I and II will be examined together in view of the elected SEQ ID NO: 1, 2, 187 and 188, elected in the response filed November 5, 2007.
2. Claims 1-20 will be examined.

Information Disclosure Statement

3. The information disclosure statements (IDSs) submitted on December 19, 2005, January 22, 2007 and May 7, 2007 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

Sequence Rules Compliance

4. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132.

APPLICANT IS GIVEN time of response to this Office Action WITHIN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 C.F.R.. §§ 1.821-1.825. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R.

§ 1.136. In no case may an applicant extend the period for response beyond the six month statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Applicants submitted a paper copy and a computer readable copy of the sequence listing, but did not provide a letter stating that the two copies are the same.

Claim Rejections - 35 USC § 112

5. Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-18 are indefinite in claim 1. Claim 1 is indefinite over the recitation of "(c) bringing into contact in each of a plurality of reaction chambers an amplicon from a different one of the amplification reactions and one or more internal sequencing primers corresponding to the amplicon". It is not clear what is meant by "an amplicon from a different one of the amplification reactions". Is it the amplicon which was obtained in that reaction chamber or is it now being added to a different reaction chamber containing another amplicon?

Claim Interpretation

6. The phrase "bringing into contact in each of a plurality of reaction chambers an amplicon from a different one of the amplification reactions and one or more internal sequencing primers corresponding to the amplicon" from claim 1 is interpreted as adding sequencing primers to amplicons generated in step (b) of claim 1.

7. The term "reaction chamber" has not been defined by Applicants, therefore it is interpreted as any support or substrate on which the amplification takes place.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 2, 4-6, 9-13 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Gibbs et al. (Genomics, vol. 7, pp. 235-244, 1990; cited in the IDS) as evidenced by Gibbs-2 et al. (PNAS USA, vol. 86, pp. 1919-1923, 1989).

Regarding claim 1, Gibbs et al. teach a method of characterizing a nucleic acid region, the method comprising:

(a) adding to each of a plurality of reaction chambers a nucleic acid sample and a different set of amplification primers, wherein each set of amplification primers is complementary to a single amplicon of a nucleic acid region of interest (page 236, paragraphs 2 and 3; Fig. 1);

(b) performing amplification reactions for each reaction chamber under the same reaction conditions (page 236, paragraphs 2 and 3);

(c) bringing into contact in each of a plurality of reaction chambers an amplicon from a different one of the amplification reactions and one or more internal sequencing primers corresponding to the amplicon (page 237, second paragraph, citing Gibbs et al., 1989a (quoted as Gibbs-2). As evidenced by Gibbs-2 et al., the sequencing reactions were performed in separate reaction tubes (page 1920, third and fourth paragraphs) with primers specific for the amplicons.);

(d) performing sequencing reactions for each reaction chamber under the same reaction conditions (see Gibbs-2 et al., page 1920, paragraphs 3-5); and

(e) analyzing the sequences of the amplicons (page 237, fourth paragraph).

Regarding claim 2, Gibbs et al. teach a multi-exon gene HPRT (hypoxanthine phosphoribosyltransferase) (Abstract; page 236, third paragraph; Fig. 1).

Regarding claim 4, Gibbs et al. teach that the amplicons collectively comprise all of the nine exons of the gene (Fig. 1; page 237, last paragraph; page 238, first paragraph).

Regarding claim 5, Gibbs et al. teach that each amplicon comprises an exon (Fig. 1; page 237, last paragraph; page 238, first paragraph).

Regarding claim 6, Gibbs et al. inherently teach generating at least 30 amplicons, as they teach 25 PCR cycles (page 236, third paragraph).

Regarding claim 9, Gibbs et al. teach PCR amplification and cycle sequencing reactions (page 236, third paragraph; page 237, second paragraph, citing Gibbs et al., 1989a (quoted as Gibbs-2) and third paragraph. As evidenced by Gibbs-2 et al., the sequencing reactions were cycle sequencing reactions (page 1920, paragraphs 3-5).

Regarding claim 10, Gibbs et al. teach purification of the amplification products prior to sequencing and purification of sequencing reaction products (page 237, second and third paragraph; Gibbs-2 et al., page page 1920, paragraphs 3-5).

Regarding claim 11, Gibbs et al. teach electrophoretic separation and fluorescent nucleotide detection (page 237, third paragraph).

Regarding claims 12 and 13, Gibbs et al. teach identifying point mutations, frameshifts and deletions (page 239, last paragraph; page 240; Fig. 3; Fig. 6).

Regarding claim 18, Gibbs et al. teach comparing the amplicon sequences to normal HPRT sequence (page 239, second paragraph).

10. Claims 1-13 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Buzin et al. (Biotechniques, vol. 28, pp. 746-748, 750, 752, 753, 2000), as evidenced by Applied Biosystems User Bulletin for CTALYST 800/877 Integrated Thermal Cycler (page 1, 12, 13 and 36, 2001).

Regarding claim 1, Buzin et al. teach a method of characterizing a nucleic acid region, the method comprising:

(a) adding to each of a plurality of reaction chambers a nucleic acid sample and a different set of amplification primers, wherein each set of amplification primers is complementary to a single amplicon of a nucleic acid region of interest (page 236, paragraphs 2 and 3; Fig. 1);

(b) performing amplification reactions for each reaction chamber under the same reaction conditions (page 747, last paragraph; page 748, paragraphs 1-3; since 384 reactions were amplified simultaneously, Buzin et al. inherently teach this limitation);

(c) bringing into contact in each of a plurality of reaction chambers an amplicon from a different one of the amplification reactions and one or more internal sequencing primers corresponding to the amplicon (page 750, second paragraph);

(d) performing sequencing reactions for each reaction chamber under the same reaction conditions (page 750, second paragraph; since 384 reactions were amplified simultaneously, Buzin et al. inherently teach this limitation); and

(e) analyzing the sequences of the amplicons (page 750, Table 2).

Regarding claims 2 and 3, Buzin et al. teach a multi-exon genes factor VIII and ATM (ataxia telangiectasia) (Abstract; page 747, fourth paragraph).

Regarding claim 4, Buzin et al. teach that the amplicons collectively comprise all of the 26 exons of factor VIII gene and all of the 66 exons of ATM gene (page 747, last paragraph; page 748, first and second paragraphs).

Regarding claim 5, Buzin et al. teach that each amplicon comprises an exon (page 747, last paragraph; page 748, first and second paragraphs).

Regarding claim 6, Buzin et al. inherently teach generating at least 30 amplicons, as they teach amplification by PCR (page 748, third paragraph).

Regarding claim 7, Buzin et al. teach performing amplification on a 384-well microplate of the ABI PRISM 877 thermocycler (page 748, third paragraph).

Regarding claim 8, Buzin et al. teach performing amplification in the ABI PRISM 877 thermocycler (page 748, third paragraph). As evidenced by the ABI PRISM 877 User Bulletin (page 13), the cycler used either 96-well plates or 384-well plates, therefore Buzin et al. inherently teach 96-well plates.

Regarding claim 9, Buzin et al. teach PCR amplification and cycle sequencing reactions (page 748, third paragraph; page 750, second paragraph).

Regarding claim 10, Buzin et al. teach purification of the amplification products prior to sequencing and purification of sequencing reaction products (page 750, second paragraph, where the PCR amplicons were extracted from a gel; further, since fluorescent cycle sequencing requires purification of the sequencing amplicons from unincorporated primers and labeled nucleotides, by teaching fluorescence cycle sequencing Buzin et al. inherently teach purification of the sequencing products).

Regarding claim 11, Buzin et al. teach electrophoretic separation and fluorescent nucleotide detection (page 750, second paragraph).

Regarding claims 12 and 13, Buzin et al. teach identifying point mutations, frameshifts and deletions (page 747, fifth paragraph).

Regarding claim 18, Buzin et al. teach detecting mutations, therefore they inherently teach comparing the amplicon sequences to normal sequences (page 747, fifth and sixth paragraph).

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. Claims 3, 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buzin et al. (Biotechniques, vol. 28, pp. 746-748, 750, 752, 753, 2000) and Bennett et al. (BMC Genetics, vol. 2:17, pp. 1-12, October 2001).

A) Regarding claim 3, Buzin et al. teach multi-exon gene ATM, but do not teach dystrophin.

B) Regarding claims 3, 16 and 17, Bennett et al. teach detection of mutations in the dystrophin gene obtained from patents with DMD (Abstract; page 2, third paragraph; Table 2).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the dystrophin gene of Bennett et al. in the analysis of mutations of Buzin et al. The motivation to do so, provided by Bennett et al., would have been that the gene was very large, with 79 exons (Abstract; page 2, first paragraph), and therefore had a high rate of mutations, of which 35% are presumed to be point mutations. as stated by Bennett et al. (page 2, first paragraph):

“These mutations have remained undetected in most patients, both male and female, because available techniques are relatively expensive and laborious given the size of the dystrophin gene.”

The motivation to do so, provided by Buzin et al., would have been, as stated by Buzin et al. (page 753, second paragraph):

“The strongest advantages of the DOVAM-S method include the parallel analysis of 45–50 samples using multiple amplified products per gel lane, and the increase in sensitivity of mutation detection to approximately 100% provided by the redundancy of the five different electrophoretic conditions. DOVAM-S is a robust method for scanning genomic DNA, particularly in large genes with widely separated exons and mutations scattered throughout the gene.”

13. Claims 3, 14 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buzin et al. (Biotechniques, vol. 28, pp. 746-748, 750, 752, 753, 2000), Bennett et al. (BMC Genetics, vol. 2:17, pp. 1-12, October 2001), GenBank Accession No. M32058 (November 1994) and Buck et al. (Biotechniques, vol. 27, pp. 528-536, 1999).

A) Regarding claim 3, Buzin et al. teach multi-exon gene ATM, but do not teach dystrophin.

B) Regarding claim 3, Bennett et al. teach detection of mutations in the dystrophin gene obtained from patients with DMD (Abstract; page 2, third paragraph; Table 2).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the dystrophin gene of Bennett et al. in the analysis of mutations of Buzin et al. The motivation to do so, provided by Bennett et al., would have been that the gene was very large, with 79 exons (Abstract; page 2, first paragraph), and therefore had a high rate of mutations, of which 35% are presumed to be point mutations. as stated by Bennett et al. (page 2, first paragraph):

“These mutations have remained undetected in most patients, both male and female, because available techniques are relatively expensive and laborious given the size of the dystrophin gene.”

The motivation to do so, provided by Buzin et al., would have been, as stated by Buzin et al. (page 753, second paragraph):

“The strongest advantages of the DOVAM-S method include the parallel analysis of 45–50 samples using multiple amplified products per gel lane, and the increase in sensitivity of mutation detection to approximately 100% provided by the redundancy of the five different electrophoretic conditions. DOVAM-S is a robust method for scanning genomic DNA, particularly in large genes with widely separated exons and mutations scattered throughout the gene.”

C) Bennett et al. teach amplifications of dystrophin exons, but do not teach primers with SEQ ID NO: 1, 2, 187 and 188.

D) GenBank Accession No. M32058 teaches exon 1 sequence of the dystrophin gene. SEQ ID NO: 1 is 100% identical to bp 139-158 of the sequence, SEQ ID NO: 2 is 100% identical to bp 1339-1362 of the sequence, SEQ ID NO: 187 is 100% identical to bp 648-669 of the sequence and SEQ ID NO: 188 is 100% identical to bp 1220-1243 of the sequence (see the enclosed sequence alignment).

Therefore it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have chosen the primers for amplification of exon 1 from the known sequence with GenBank Accession No. M32058 with a reasonable expectation of success, since a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties.

Buck et al. expressly provide evidence of the equivalence of primers. Specifically, Buck et al. invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck et al. also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck et al. tested

each of the primers selected by the methods of the different labs, Buck et al. found that EVERY SINGLE PRIMER worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (see page 533, column 1). Buck et al. expressly state "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck et al. provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

14. Claims 19 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over GenBank Accession No. M32058 (November 1994) and Buck et al. (Biotechniques, vol. 27, pp. 528-536, 1999).

A) GenBank Accession No. M32058 teaches exon 1 sequence of the dystrophin gene. SEQ ID NO: 1 is 100% identical to bp 139-158 of the sequence, SEQ ID NO: 2 is 100% identical to bp 1339-1362 of the sequence, SEQ ID NO: 187 is 100% identical to bp 648-669 of the sequence and SEQ ID NO: 188 is 100% identical to bp 1220-1243 of the sequence (see the enclosed sequence alignment).

Therefore it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have chosen the primers for amplification of exon 1 from the known sequence with GenBank Accession No. M32058 with a reasonable expectation of success, since a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties.

Buck et al. expressly provide evidence of the equivalence of primers. Specifically, Buck et al. invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck et al. also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck et al. tested each of the primers selected by the methods of the different labs, Buck et al. found that EVERY SINGLE PRIMER worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (see page 533, column 1). Buck et al. expressly state "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck et al. provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

15. No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E. Strzelecka whose telephone number is (571) 272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Teresa E Strzelecka
Primary Examiner
Art Unit 1637

Teresa Strzelecka
1/19/08

Notice to Comply

Application No.

10/539,178

Examiner

Teresa E. Strzelecka

Applicant(s)

FLANIGAN ET AL.

Art Unit

1637

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- ☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- ☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- ☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- ☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- ☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- ☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- ☒ 7. Other: There is no letter stating that the paper and computer readable copies of the sequence listing are the same.

Applicant Must Provide:

- ☐ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- ☐ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- ☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216

For CRF Submission Help, call (703) 308-4212

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